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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,264	06/22/2001	Sean H. Adams	11669.187USU1	8727

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MERCHANT & GOULD PC
P.O. BOX 2903
MINNEAPOLIS, MN 55402-0903

EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,264	ADAMS ET AL.	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,28,34-41,43,44,46,52-58 and 74-76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,28,34-41,43,44,46,52-58 and 74-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/20/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 9/20/04.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/20/04 has been entered. Claims 1, 28, 34-41 43, 44, 46, 52-58 and 74-76 are currently pending and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/20/04 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 28, 34-41 43, 44, 46, 52-58 and 74-76 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A method for screening for compounds that affect mitochondrial uncoupling wherein the method comprises contacting a mammalian cell or tissue sample with a candidate compound in vitro; analyzing expression of an 2-oxoglutarate carrier (OGC) polypeptide in the mammalian cell or tissue sample contacted with the candidate compound wherein said OGC polypeptide is at least 95% identical to the polypeptide encoded by SEQ ID NO:1 or SEQ ID NO:2 and has mitochondrial uncoupling activity; analyzing mitochondrial membrane potential in said mammalian cell or tissue sample contacted with the candidate compound; wherein a change in the expression of the OGC polypeptide and a change in mitochondrial membrane potential relative to a control cell indicates that the candidate compound affects mitochondrial uncoupling;

does not reasonably provide enablement for the full scope encompassed by the claims. Specifically, the claims are not enabled for screening for compounds that after any type of "uncoupling" other than "mitochondrial uncoupling" or for a screening method that is performed in vivo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to methods of identifying compounds that affect uncoupling. As such, the nature of the invention is a biochemical screening assay.

The breadth of the claims

The instant claims are very broad. For instance, the claims encompass screening for compounds that affect any type of uncoupling. A indicates below, there are different types of uncoupling recognized in the art. Since the claims only indicate that the method is for identifying compounds that affect uncoupling, the claims encompass screening for compounds that affect any type of uncoupling. Additionally, the claims do not limit the method to an in vitro method. Looking to the specification for guidance, it is clear that the specification contemplates that the method can be either in vitro or in vivo (e.g., see p. 19, lines 6-26). As such the claims encompass a method that can be performed on cells or tissues that are either in vitro or in vivo. Furthermore, the method steps of analyzing polypeptide expression and analyzing mitochondrial membrane potential do not indicate that the expression level and membrane potential are analyzed in the cell that is contacted with the candidate compound; therefore, the claims encompass analyzing polypeptide expression and mitochondrial membrane potential in a cell/tissue other than the cell/tissue that is contacted by the candidate compound.

The unpredictability of the art and the state of the prior art

As indicated above, the claims are drawn to methods of identifying compounds that affect uncoupling. However, the claims do not specifically indicate the specific type of uncoupling. It is respectfully pointed out that the prior art (e.g., see Guo et al. American Journal of Physiology, 1999; Daniel et al. Neurogastroenterol. Mot., 2001) indicates that gap junctions are involved in "coupling" and that inhibitors can be used to "uncouple" the gap junction coupling. Specifically, Guo teaches, "[I]n nervous tissue and the myocardium, gap junctions establish low-resistance channels that couple cells electrically, permitting a rapid and synchronous response to diverse stimuli" (see p.L1018, right column); and, "In alveolar epithelial cells, acute exposure to 18alpha-GA at a low concentration caused a rapid and reversible uncoupling of GJIC" (see p. L1024, right column). Also, Daniel teaches "The objective of this study was to use uncouplers of gap junctions, 18alpha-glycyrrhetenic acid and its water soluble analogue carbenoxolone, to evaluate if gap junctions function in pacing and neurotransmission." (See abstract). Therefore, it is clear that the prior art teaches, and thus one of skill in the art would be aware that there are different types of "coupling" and thus different types of "uncoupling".

Working Examples and Guidance in the Specification

It is acknowledged that the specification contains an example wherein human OGC was overexpressed in 293 cells, resulting in the decreasing mitochondrial membrane potential (see example 1, p.48). It is noted that it appears that the 293 cells are in vitro in Example 1. Furthermore, the mitochondrial membrane potential was measured in the 293 cells that were contacted with the candidate compound. As such, the Example sets forth the basis for the notion

that OGC is associates with mitochondrial membrane potential (and thus, mitochondria coupling).

Quantity of Experimentation

Considering the breadth of the claims, indicated above, it is determined that in order for one of skill in the art to be able to make and use the claimed invention to the full breadth encompassed by the claims, additional experimentation would first be required. For instance, the claims encompass identifying a compound that affects any type of uncoupling. Considering that the art recognizes that there are different types of "coupling"/"uncoupling", additional experimentation would be required to first establish that OGC was involved with non-mitochondrial coupling. For instance, OGC would have to be associated with gap junction coupling/uncoupling. Since the specification indicates that OGC is a mitochondrial protein (i.e. it is found in the mitochondria of cells) and since the specification and prior art do not recognize that OGC is associated with gap junctions, the amount of additional experimentation required is considered undue. Furthermore, additional experimentation would be required in order to show that the method would work when the expression level and mitochondrial membrane potential are analyzed in cells other than the cells that are contacted by the compound. Since there is no indication that the compound can have an affect on a cell that is not contacted, the amount of additional experimentation to show that the method could work when the expression level and membrane potential are analyzed in cell other than the cell that is contacted by the compound. Finally, the claims encompass a method wherein the method is performed on cells/tissues wherein the cells/tissues are in vivo (i.e., an in vivo method). Looking to the specification for

guidance, there are no working examples that indicate how to perform the method in vivo. Furthermore, there is no guidance for how to analyze protein expression and mitochondrial membrane potential on cells that are in vivo. The prior art does not appear to recognize any methods wherein the level of protein expression and mitochondrial membrane potential can be analyzed in vivo. The only methods known (including the present disclosure) were for analyzing protein levels and mitochondrial membrane potential in vitro. Therefore, the amount of additional experimentation required to be able to make and use the methods in vivo is undue.

Level of the skill in the art

Considering that the nature of the invention, is a biochemical assay that is usually performed by individual with a high degree of educational and/or technical training in biochemistry, the level of the skill in the art is deemed to be high.

Conclusion

Considering the nature of the invention, the breadth of the claims, the limited working examples and guidance provided by the specification, and the high degree of skill required, it is concluded that the amount of additional experimentation required to perform the broadly claimed invention is undue.

Response to Arguments

Applicant's arguments, see communication filed 9/20/04, with respect to the rejection(s)of claim(s) under 35 USC 112, 1st paragraph (Written description) have been fully considered and are persuasive. It is acknowledged that there are other variant forms of OGC that are known in the art that are at least 95% identical to human OGC. Furthermore, the art recognized that the proteins that are "carrier proteins" which are encompassed by the claims

comprise three functional domains. Therefore, the specification has adequately described a "representative number" of species encompassed by the claims and made a reasonable structure/function relationship for the claimed species. Therefore, the rejection has been withdrawn.

However, upon further consideration, a new ground(s) of rejection for the reasons indicated herein.

Miscellaneous

It is noted that amending the claims as indicated in the enablement rejection would overcome the rejection and the claims would be allowable.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon Eric Angell, Ph.D.
Art Unit 1635

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